Patient NCCN Risk Classification Based on Combined Clinical Cell Cycle Risk (CCR) Score

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Abstract 249

BACKGROUND

- Improved prognostic tools for newly diagnosed prostate cancer are needed to more appropriately match treatment to a patient's risk of progression.
- The cell cycle progression (CCP) score is a highly validated prognostic RNA expression signature which has been combined with CAPRA[1] (CCR, combined clinical cell cycle risk score) to generate an estimate of prostate cancer mortality (PCM) within 10-years of diagnosis.[2,]
- Here, we evaluate how the prognostic information from CCR can reclassify a patient's risk compared to their initial assignment to an NCCN risk category based on clinicopathologic features alone.

METHODS

COHORT

- A risk reclassification scheme was applied to patients tested by the Myriad Genetics commercial laboratory (N=16,442).
- Clinicopathological data was obtained from physician-completed test request forms. This does not include outcomes data.

CCP TESTING

- Formalin-fixed paraffin-embedded biopsy samples were analyzed for the expression of 46 genes (31 CCP genes and 15 housekeeping genes).[3]
- The CCP score is an unweighted average of the CCP genes normalized by the average expression of the housekeeping genes.
- The CCR score was previously validated and is calculated as a linear combination of CAPRA and CCP score (0.39 x CAPRA + 0.57 x CCP).[2]

ANALYSIS

- PCM risk was assigned based on the patient's CCR score. NCCN risk category[4] was assigned using the clinicopathologic data from the test request form. Men in the NCCN very low and low risk categories were grouped together.
- Patients whose PCM risks were outside the interquartile range (IQR) of their NCCN risk category were reclassified according to whether their PCM risks fell within the IQR of another NCCN risk category (Table 1).

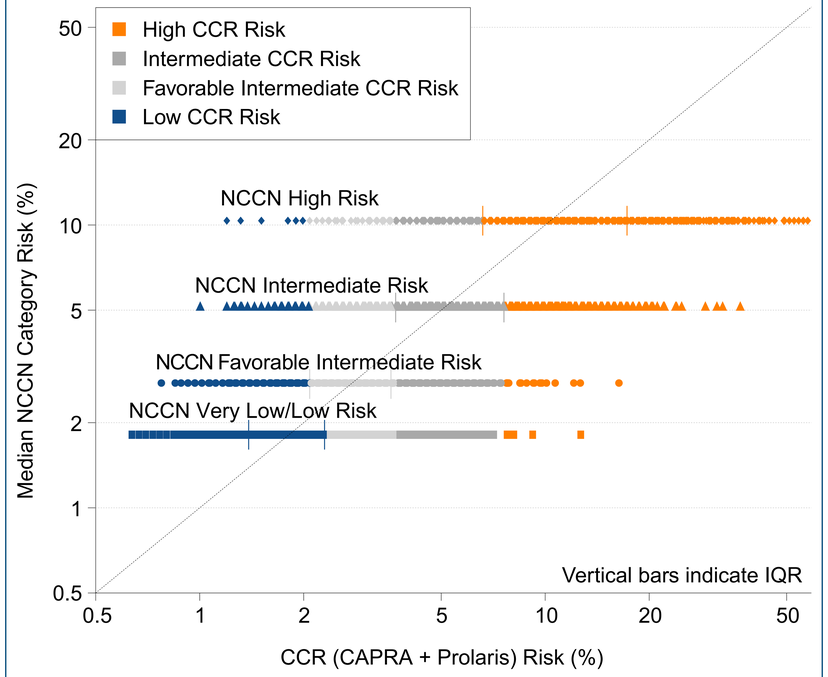
Table 1. Reclassification Examples

	Example 1	Example 2
NCCN Risk	Low Risk	Intermediate Risk
PCM risk as determined by CCR	Below Upper Limit of IQR for NCCN Low Risk	Below Upper Limit of IQR for NCCN Low Risk
Reclassification	None	Reclassified - Low Risk

RESULTS

- Based on clinicopathologic features alone, men in this cohort were classified according to NCCN guidelines as very low/low (n=8,695), favorable intermediate (n=3,347), intermediate (n=3,086), or high risk (n=1,224).
- Table 2 and Figure 1 show the results of calculating patient risk of PCM based on CCR in the commercially tested patients (N=16,442).

Figure 1. CCR Reclassification of PCM in Commercial Cohort (N=16,442)



Scatter plot showing the predicted risk of PCM based on clinicopathologic features alone (y-axis) versus CCR risk (x-axis).

- After calculating patient risk of PCM based on CCR, 11.4% of all men were reclassified to a lower risk category and 22.6% of men were reclassified to a higher risk category.
  - NCCN very low/low risk category: 25% reclassified to favorable intermediate or intermediate risk
  - NCCN favorable intermediate risk category: 24% reclassified to lower risk and 23% to higher risk
  - NCCN intermediate risk category: 24% reclassified to lower and 25% to higher risk
  - NCCN high risk category: 25% reclassified to favorable intermediate or intermediate risk

Table 2. CCR Reclassification of PCM in Commercial Cohort (N=16,442)

	LOW	FAVORABLE INTERMEDIATE	INTERMEDIATE	HIGH
NCCN Very Low/Low (n=8,695)	6,544 (75%)	1,820 (21%)	325 (4%)	6 (<1%)
NCCN Favorable Intermediate (n=3,437)	808 (24%)	1,833 (53%)	772 (22%)	24 (1%)
NCCN Intermediate (n=3,086)	106 (3%)	658 (21%)	1,558 (50%)	764 (25%)
NCCN High (n=1,224)	6 (<1%)	46 (4%)	251 (21%)	921 (75%)
TOTAL	7,464	4,346	2,917	1,715

CONCLUSIONS

- The prognostic information in the CCR score results in significant amounts of risk reclassification for all patients with localized disease when compared to stratification based only on NCCN risk categories.
- This additional information can be used to more appropriately guide medical management.

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Please email Steven Stone (steve@myriad.com) with any questions or comments.

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